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Imaging Findings of SARS-CoV-2 Infection in Pediatrics: A Systematic Review of Coronavirus Disease 2019 (COVID-19) in 850 Patients

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Rationale and objectives: Children with COVID-19 seem to have a relatively milder disease and better prognosis; however, severe disease or death could still occur in this age group. Although the knowledge on the clinical and epidemiology of COVID-19 in pediatric patients is being accumulated rapidly, relevant comprehensive review on its radiological manifestations is still lacking. The present article reviews the radiological characteristics of COVID-19 in pediatrics, based on the previous studies.

Materials and methods: We conducted a systematic literature search for published articles by using Medline, Scopus, Google Scholar and Embase online databases. All studies describing CT findings of COVID-19 in pediatrics (<18years) were included.

Results: A total of 39 studies with 850 pediatric patients were reviewed. 225 (26.5%) of patients had normal CT findings. Ground-glass opacities and consolidations were the most common CT abnormalities (384/625, 61.5%). Other findings were halo sign, interstitial opacities, bronchial wall thickening, and crazy-paving sign. Approximately 55% of patients had unilateral pulmonary findings. Most studies found peripheral and lower-lobe distribution to be a prominent imaging finding.

Conclusion: Our study showed that imaging findings in children were often milder and more focal than adults, typically as ground-glass opacities and consolidations with unilateral lower-lobe predominance, which have been regressed during the recovery time. A balance must be struck between the risk of radiation and the need for chest CT. If still necessary, low-dose CT is more appropriate in this age group. Albeit, due to the limited number of reported pediatrics with COVID-19, and the lack of consistency in CT descriptors, further work is still needed in this regard.

Key Words: COVID-19; SARS-CoV-2; Pneumonia; Children; Pediatrics; Chest imaging; CT-scan; Lung; Radiation.

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INTRODUCTION

In late December 2019, an outbreak of novel coronavirus, called Coronavirus Disease 2019 (COVID-19), emerged in Wuhan (China), which was later declared as a global pandemic by the World Health Organization (WHO). As of August 2, 2020, more than 18 million cases of COVID-19

with above 690,000 deaths have been confirmed in more than 200 countries and territories [1].

In the early publications, no infected children younger than fifteen years old was reported, and it was thought that children were not susceptible to COVID-19 [2]. With the progression of the outbreak and the subsequent increase in the number of infected adult contacts, the number of pediatric infections increased concomitantly, and later studies revealed that COVID-19 pneumonia could in fact affect all ages [3,4]. However, there are still relatively few reported cases of SARS-CoV-2 infection in children compared to adults. Moreover, children with COVID-19 infection usually have a milder illness and a better prognosis [5]. The largest pediatric COVID-19 study by Dong Y et al. on 2143 children with confirmed or suspected infection revealed that most pediatric patients (94.1%) were asymptomatic or had mild to moderate disease [6]. In this report, 13% of laboratory-confirmed cases were asymptomatic. Since many children without symptoms are unlikely to be tested, the true

Acad Radiol 2020; 27:1608–1621

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<https://doi.org/10.1016/j.acra.2020.07.031>

rate of asymptomatic infection is almost certainly higher. Due to their pivotal role in viral transmission and replication of SARS-CoV-2 [7-9], infected pediatric patients should be monitored closely as a means of preventing the disease spread. Although the information on the epidemiology of COVID-19 in pediatric patients is being accumulated, relevant comprehensive literature on its diagnosis, including the radiological manifestations, are lacking. Unlike the adults, studies describing the chest imaging manifestations of COVID-19 in pediatric patients have been limited to date. Therefore, the present systematic review describes the radiological characteristics of COVID-19 in pediatric population.

MATERIALS AND METHODS

Search strategy

The research question used was: “What are the diagnostic features of COVID-19 infection in chest CT of pediatric

TABLE 1. Frequency of Chest CT findings in pediatric COVID-19

CT Findings	Pooled values
GGO*	205
Patchy consolidations	156
Mixed (GGO and consolidation)	23
Normal	225

* Ground-glass opacities

population?” We conducted a systematic literature search for published articles describing relevant imaging findings by using Medline (used by PubMed), Google Scholar, Scopus and Embase online databases. The studies were chosen by using the following search terms: “COVID-19”; OR “SARS-CoV2” AND “pediatrics” OR “children” AND “computed tomography” OR “CT-scan”. We also searched references from several articles to find any possible additional studies that reported chest CT findings of COVID-19 in

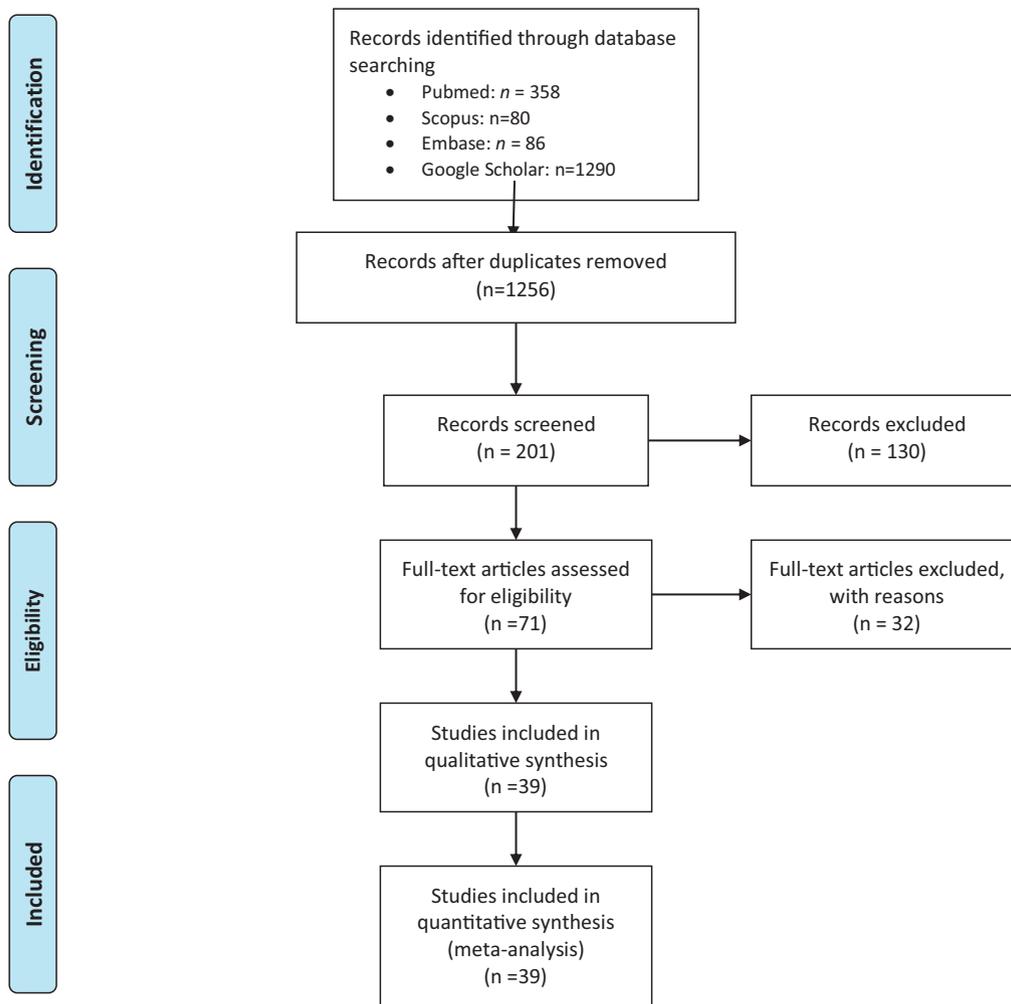


Fig. 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram. Diagram represents the review process and selection of included studies. Embase is a product of Elsevier. WHO = World Health Organization. Adapted from. Moher et al. (doi.org/10.1371/journal.pmed.1000097) ©2009, under terms of Creative Commons Attribution 4.0 International License (creativecommons.org/licenses/by/4.0/legalcode). (Color version of figure is available online.)

TABLE 2. The NIH quality assessment tool for case series studies.

First Author [Reference No]	Questions									Overall Rating	Case Number
	1	2	3	4	5	6	7	8	9		
Lu X [10]	Yes	Yes	NR	CD	Yes	Yes	CD	No	Yes	Fair	171
Li W [21]	Yes	Yes	Yes	CD	Yes	Yes	CD	NA	Yes	Fair	5
Liu H [22]	Yes	Yes	Yes	CD	Yes	Yes	CD	NA	Yes	Good	4
Xia W [16]	Yes	Yes	NR	CD	Yes	Yes	CD	Yes	Yes	Fair	20
Yang P [12]	Yes	NR	NR	NR	CD	NR	CD	NR	No	Poor	134
Wang D [20]	Yes	Yes	NR	CD	Yes	Yes	CD	Yes	Yes	Fair	31
Feng K [17]	Yes	Yes	NR	NR	Yes	Yes	CD	Yes	Yes	Fair	15
Rahimzade G [18]	Yes	Yes	CD	NR	Yes	Yes	CD	NA	Yes	Fair	9
Zhu L [30]	Yes	Yes	NR	CD	Yes	Yes	CD	NA	Yes	Fair	10
Zhou Y [31]	Yes	Yes	CD	CD	Yes	Yes	CD	NR	Yes	Fair	9
Sun D [25]	Yes	Yes	NR	CD	Yes	Yes	CD	Yes	Yes	Fair	8
Shen Q [32]	Yes	Yes	NR	NR	Yes	Yes	CD	Yes	Yes	Fair	9
Qiu H [26]	Yes	Yes	NR	NR	Yes	Yes	CD	Yes	Yes	Fair	36
Li B [24]	Yes	Yes	NR	Yes	Yes	Yes	CD	Yes	Yes	Fair	22
Liu W [33]	Yes	Yes	NR	Yes	Yes	Yes	CD	NA	Yes	Fair	6
Xu H [19]	Yes	Yes	NR	NA	Yes	Yes	CD	NA	Yes	Fair	2
Tang A [13]	Yes	Yes	NR	NA	Yes	Yes	CD	CD	Yes	Fair	26
Pan X [36]	Yes	Yes	NA	NA	Yes	Yes	CD	NA	Yes	Fair	1
Liu [37]	Yes	Yes	NA	NR	Yes	Yes	CD	NA	Yes	Fair	5
Lou MX [38]	Yes	Yes	NA	NR	Yes	Yes	CD	NA	No	Fair	3
Hu Z [40]	Yes	Yes	NA	NR	Yes	Yes	CD	Yes	Yes	Fair	24
Xie M [41]	Yes	Yes	NA	NR	Yes	Yes	CD	Yes	CD	Fair	13
Wang S [42]	Yes	Yes	NA	NA	Yes	Yes	CD	NA	Yes	Good	1
Tan YP [43]	Yes	Yes	NA	NR	Yes	Yes	CD	Yes	Yes	Fair	10
Chen A [44]	Yes	Yes	NA	NR	Yes	Yes	CD	Yes	Yes	Fair	14
Zheng F [45]	Yes	Yes	NA	NR	Yes	Yes	CD	Yes	Yes	Fair	25
An P [46]	Yes	Yes	NA	NA	No	CD	CD	NA	CD	Fair	1
Zhang C [47]	Yes	Yes	NR	NR	No	CD	CD	NR	NR	Fair	34
Chen J [14]	Yes	Yes	NA	NR	Yes	Yes	CD	NR	NR	Fair	12
Li Y [15]	Yes	Yes	NR	NR	No	Yes	CD	Yes	Yes	Fair	8
Jiang JY [48]	Yes	Yes	NA	NR	Yes	Yes	CD	Yes	Yes	Fair	6
Eghbali [35]	Yes	Yes	NR	NR	No	CD	CD	NR	NA	Fair	4
Chen F [11]	Yes	Yes	NA	NA	No	CD	CD	NA	CD	Fair	1
Steinberger S [54]	Yes	Yes	NA	NR	Yes	Yes	CD	Yes	CD	Good	30
Mungmunpantipantip [55]	No	No	NA	NR	No	No	CD	NA	No	Fair	3
Lai W [56]	Yes	Yes	NA	NA	Yes	CD	CD	NA	CD	Fair	2
Lan L [57]	Yes	Yes	NA	NR	Yes	CD	CD	NA	CD	Fair	4
Ma H [58]	Yes	Yes	NA	NR	Yes	Yes	CD	Yes	Yes	Good	50
Yu H [59]	Yes	Yes	NA	NR	Yes	CD	CD	NA	CD	Fair	82

NIH = National Institutes of Health, NR = not reported, CD = cannot determine, NA = not applicable

The tool poses nine questions: 1 = Was the study question or objective clearly stated? 2 = Was the study population clearly and fully described, including a case definition? 3 = Were the cases consecutive? 4 = Were the subjects comparable? 5 = Was the intervention clearly described? 6 = Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? 7 = Was the length of follow-up adequate? 8 = Were the statistical methods well-described? 9 = Were the results well-described? (Source: National Heart, Lung, and Blood Institute; National Institutes of Health; U.S. Department of Health and Human Services. Xu H, Tang A, Xie M and Zhang C: preliminary data.

children. A hand search was also performed in Google search engine and Google scholar to include non-indexed reports. The search was carried out on April 5, 2020 and was updated on June 10, 2020. There was no language limitation, and the studies whose title, abstract, or body contained any of the search terms were selected. Repeated studies were excluded, as were studies whose full texts were not found in the databases consulted.

Study selection and Eligibility criteria

Two reviewers independently summarized all relevant articles. We included all studies that investigated CT scan findings of COVID-19 infection (confirmed with RT-PCR) in pediatrics (<18 years). No search filters or language restrictions were applied. Studies with no CT findings reported, no full article or those relating to other coronaviruses such as Middle East

TABLE 3. Frequency of chest CT findings in pediatric COVID-1.

Authors	Case N.	Abnormal CT	Normal CT	GGO	Consolidation	Mixed
Lu X [10]	171	144	27	56	53	-
Li W [21]	5	3	2	3	0	-
Liu H [22]	4	3	1	1	1	1
Xia W [16]	20	16	4	12	10	-
Yang P [12]	134	94	40	-	-	-
Wang D [20]	31	14	17	-	-	-
Feng K17	15	9	6	9	0	-
Rahimzade G [18]	9	8	1	0	5	3
Zhu L [30]	10	5	5	3	0	-
Zhou Y [31]	9	8	1	1	1	6
Sun D [25]	8	8	0	6	7	-
Shen Q [32]	9	2	7	2	0	-
Qiu H [26]	36	19	17	19	0	-
Li B [24]	22	20	2	3	7	8
Liu W [33]	6	4	2	1	3	-
Xu H [19]	2	2	0	1	0	-
Tang A [13]	26	18	8	0	0	-
Pan X [36]	1	0	1	0	0	-
Liu M [37]	5	4	1	3	0	1
Lou MX [38]	3	3	0	3	0	-
Hu Z [40]	24	17	7	12	0	-
Xie M [41]	13	4	9	2	2	-
Wang S [42]	1	1	0	0	1	-
Tan YP [v]	10	5	5	4	0	-
Chen A [44]	14	7	7	3	0	1
Zheng F [45]	25	17	8	0	0	-
An P [46]	1	1	0	0	1	-
chen J [14]	12	10	2	0	0	-
Li Y [15]	8	6	2	0	3	1
Chen F [11]	1	1	0	0	0	1
Eghbali A [35]	4	4	0	4	0	-
Jiang JY [48]	6	5	1	0	1	-
Zhang C [47]	34	28	6	0	33	-
Steinberger S [54]	30	7	23	6	0	1
Mungmunpantipantip R [55]	3	0	3	0	0	0
Lai W [56]	2	2	0	2	0	0
Lan L [57]	4	3	1	2	0	1
Ma H [58]	50	43	7	29	25	-
Yu H [59]	82	80	2	18	3	-
	850	625	225	205	156	23

respiratory syndrome (MERS) were excluded. The article selection process and details of the search strategy are described as a flowchart in Fig. 1, as recommended in the PRISMA statement.

Data extraction, quality assessments and management

Data was extracted by two authors. The reviewers independently summarized information with a standardized data abstraction form. Study design, number of patients, and CT findings were included in the forms. If a study included COVID-19 patients from all age groups, only data from pediatric patients (0-18) were included. Patients older than 18 years of age or those without chest CT examinations were excluded. Quality of the included studies was assessed based on the 9-items National Institutes of

Health Quality Assessment Tool for Case Series Studies [49]. The studies were assigned a quality rating of “good,” “fair,” or “poor”. The study design and presence of possible bias were utilized to evaluate the quality of studies. Studies with high risk of bias were defined as poor quality, those with moderate risk (did not affect the results) as fair quality, and the presence of minimal risk as good quality.

RESULTS

Overview of the included studies

A summary of articles included in this literature review is provided in Table 2. The electronic literature searches initially yielded 1814 articles. After manual screening of these articles based on their

TABLE 4. Chest CT findings in pediatric COVID-19. *NA: not available. **GGO: Ground-glass opacity.

Authors	Case N.	Mean Age	Findings
Lu X [10]	171	6.7y	CT <ul style="list-style-type: none"> • 60 (35%) normal • 56 (32.7%) GGO** • 32 (18.7%) local patchy shadowing • 21 (12.3%) bilateral patchy shadowing
Li W [v]	5	3.4y	CT <ul style="list-style-type: none"> • 2 (1.2%) interstitial opacities • 2 (40%) normal
Liu H [22]	4	5 y,11m, 9y,2m	CT <ul style="list-style-type: none"> • 3 (60%) patchy GGO • 1 (25%) normal • 1 (25%) consolidation • 1 (25%) single GGO at RML
Xia W [v]	20	2.1y	CT <ul style="list-style-type: none"> • 1 (25%) multifocal consolidation (pleural effusion) • 4 (20%) normal • 16 (80%) subpleural GGOs • 10 (50%) consolidation with surrounding GG halo • 12 (60%) GGOs • 4 (20%) fine mesh shadow • 3 (15%) micronodules 6 (30%) unilateral, and 10 (50%) bilateral lung lesions
Yang P [12]	134	<10y	CT
Wang D [20]	31	7.1y	CT <ul style="list-style-type: none"> • 17 (55%) normal • 9 (45%) patchy GGOs and nodules • mostly located in the lower lobe of both lungs near the pleural area
Feng K [17]	15	4-14y	CT <ul style="list-style-type: none"> • 6 (40%) normal • 9 (60) inflammatory changes (7 cases with small nodular GGOs and 2 cases had speckled GGO)
Rahimzade G [18]	9	5y	CXR CT <ul style="list-style-type: none"> • 1 (11%) normal CT • 3 (33%) air-space shadowing. patchy consolidation with halo sign and GGO in both lungs (2 with halo (• 5 (56%) air-space shadowing, patchy consolidation with halo sign in both lungs

(continued)

TABLE 4. (Continued)

Authors	Case N.	Mean Age	Findings
Zhu L [30]	10	2y	CT <ul style="list-style-type: none"> • 5 (50%) normal
Zhou Y [31]	9	0-3y	CT <ul style="list-style-type: none"> • 5 (50%; 3 unilateral, 2 bilateral) pneumonia (3 GGO) • 1 (11.1%) normal • 6 (67%) GGO+ consolidation • 1 (11.1%) consolidation • 1 (11.1%) GGO 1 (11.1%) pleural effusion, and 3 (33.3%) halo sign 4 bilateral, 4 unilateral
Sun D [25]	8	8.3y	CT <ul style="list-style-type: none"> • 7 (87%) multiple patch-like shadows • 6 (67%) GGOs, some lesions as mixed inflammatory changes
Shen Q [32]	9	6.4y	CT CXR <ul style="list-style-type: none"> • 7 (77.8%) normal • 2 (22.2%) unilateral GGO
Qiu H [26]	36	8.3y	CT <ul style="list-style-type: none"> • 17 (47%) normal • 19 (53%) GGO
Li B [24]	22	NA*	CT <ul style="list-style-type: none"> • 2 (9%) normal • 8 (36%) mixed GGO • 7 (32%) consolidation lesions • 3 (14%) GGOs • Peripheral distribution (45%) of lung lesions was predominant. Most of the lesions were multilobar (68%), with an average of 3 lung segments involved.
Liu W [33]	6	3y	CT <ul style="list-style-type: none"> • 1 (16%)normal, • 4 (66%) showed typical bilateral viral pneumonia patterns: 1 (16%) patchy GGO, 3 • (50 %) patchy shadows
Xu H [19]	2	10y, 3m	CT <ul style="list-style-type: none"> • 1 no CT • 1 nodule at RUL • 1 bilateral peripheral GGO
Tang A [13]	26	6.9y	CT CXR <ul style="list-style-type: none"> • 8 (31%) normal • 11 (42%) unilateral pulmonary infiltrates

(continued)

TABLE 4. (Continued)

Authors	Case N.	Mean Age		Findings
Pan X [36]	1	3y	CT	• 7 (27%) bilateral pulmonary infiltrates (no detailed description)
Liu M [37]	5	5.9	CT	normal
				• 1 (20%) normal
				• 3 (60%) GGO (2 unilateral, 1 bilateral)
Lou MX [38]	3	8y, 6y, 3m	CT	• 1 (20%) unilateral GGO + consolidation
Hu Z [40]	24	NA	CT	3 (100%): unilateral peripheral GGO
				• 7 (30%) normal
				• 12 (50%) GGO
Xie M [41]	13	16y	CT	• 5 (20.8%) stripe shadowing in the lungs
				• 9 (70%) normal
				• 2 (15%) GGO
Wang S [42]	1	36hours	CT CXR	• 2 (15%) patchy shadows in the lungs CXR: thickened lung texture CT: high-density nodular shadow at posterior segment of LUL
Tan YP [43]	10	NA	CT	• 5 (50%) normal
				• 4 (40%) GGO,
Chen A [44]	14	4.7y	CT	• 1 (10%) changes similar to bronchopneumonia
				• 7 (50%) normal
				• 3 (47.2%) GGO
				• 1 (14.7%) GGO+ consolidation
				• 1 (14.7%) nodule
Zheng F [45]	25	3y	CT	• 2 (28.6%) bronchial wall thickening 4 (57.1%) bilateral, 4 (57.1%) peripheral, 1 (14.3%) both central and peripheral, 2 (28.6%) peribronchial distribution
				• 8 (33%) normal
				• 5 (21%) unilateral findings
				• 11 (46%) bilateral findings
An P [46]	1	3y	CT	• Number of cases with different pattern of abnormalities not described, but bilateral patchy shadows or consolidations were stated as the most CT finding consolidation or patchy shadow

(continued)

TABLE 4. (Continued)

Authors	Case N.	Mean Age		Findings
Chen J [14]	12	14.5y	CT	<ul style="list-style-type: none"> • 2 (17%) normal • 10 (83%) abnormal CT. GGO and local patchy shadowing were the typical radiological findings on chest CT scan (no more details) • 1 tiny shadow of fibrotic streaks in the right lung (not COVID-related)
Li Y [15]	8	2.6y	CT	<ul style="list-style-type: none"> • 1 (12.5%) normal, 1 (12.5%) rather normal (minimal pleural thickening) • 1 (12.5%) consolidation (subpleural RUL) • 1 (12.5%) multiple consolidation and, and a “halo sign” appearance • 1 (12.5%) bronchial pneumonia-like changes in LUL, with multiple high-density • nodular shadows and GGO along the bronchovascular bundles • 2 (25%) asthmatic bronchitis-like changes. • 1 (12.5%) bronchial pneumonia-like changes in the bilateral lungs, as multiple patchy shadows scattered
Chen F [11]	1	NA	CT	Large consolidation with GGO in the right lung
Eghbali A [35]	4	11y	CT	
Jiang JY [48]	6	NA	CXR	4 (100%): subpleural GGOs
			CT	<ul style="list-style-type: none"> • 1 (25%) normal • 2 (34%) typical COVID-19 findings • 3 (50%) atypical findings
Zhang C [47]	34	33m	CT	<ul style="list-style-type: none"> • 6 (18%) normal • On admission, there were 14 (41.18%) bilateral and 14 (41.18%) unilateral patchy lesions. After 5 days, 5 more cases got abnormal CTs (no detail)
Steinberger S [54]	30	10y	CT	<ul style="list-style-type: none"> • 23 (77%) normal • 1 (14%) GGOs and consolidation • 6 (86) GGOs only • 0 (0) consolidation only
Mungmunpantipantip R [55]	3	NA	CT	5 (71%) more than two lobes affected, 5 (71%) bilateral lung disease
Lai W [56]	2	12y, 16y	CT	3 (100%) normal - 2 (100%) GGOs* Case 1: normal first scan (4 days after symptom onset) was normal.

(continued)

TABLE 4. (Continued)

Authors	Case N.	Mean Age	Findings
Lan L [57]	4	9.7y	CT
			<ul style="list-style-type: none"> • Repeat examination after 4 more days showed multiple patches of subpleural GGO • Case 2: patchy GGO and vascular dilatation in the left upper lobe in CT on day 2 after admission • 1 (25%) normal • Amongst the 3 (75%) abnormal CT, 5 lesions were found: 4GGO (3 pure GGO, mixed), 1 consolidation • Delicate interstitial thickening was observed in 1 pure GGO • 2 unilateral, 1 bilateral lung involvement in CT scans
Ma H [58]	50	3y	CT
			<ul style="list-style-type: none"> • 29 (67%) GGOs • 16 (37%) localized patchy shadowing • 9 (21%) bilateral patchy shadows • 3 (7%) interstitial opacities • 1 (2%) pleural effusion
Yu H [59]	82	3d-16y	CT CXR
			<ul style="list-style-type: none"> • 2 (2.44%) normal CT • 38 (46.34%) unilateral pneumonia • 30 (36.59%) bilateral pneumonia • 18 (21.95%) multiple mottling and GGO • 3 (3.61%) Partial pulmonary consolidation • 1 (1.22%) pleural effusion • 12 (14.63%) lung texture enhancement

titles and abstracts, a total of 39 studies reporting imaging findings for 850 individuals met the inclusion criteria for this systematic review. Four studies were case reports and the others were designed as case series. Most of the included studies were from China. CT imaging was evaluated in all studies and chest X-ray data had been added occasionally. Sample sizes were small in most of the included studies as expected, due to the rarely reported pediatric COVID-19 cases worldwide. The methodological quality of the studies was mostly rated as fair.

Chest CT manifestations

CT abnormalities and characteristic patterns

Various CT findings of pediatric COVID-19 cases have been described in several studies (Tables 3,4). After combining the

available data, we found 625 (73.5%) patients to have abnormal CT findings (Table 1). Several studies have reported that most infected children will display abnormal findings in chest CT imaging. This contradicts the findings of a few studies, notably a recent study by Steinberger et al. [54], who has reported that most COVID-19 children (77%) have normal CT findings.

Amongst the abnormal CT findings, the characteristic patterns of isolated ground-glass opacification (GGO, 32%), consolidations (25%), or a combination of GGO and consolidative opacities (3.7%), were the most common features in pediatric population with COVID-19 (Tables 1,3,4). Other reported findings were halo sign, undetermined interstitial changes [10], bronchial pneumonia-like changes [15], pulmonary nodules [16,19,20], bronchial wall thickening, and crazy-paving sign.

Unfortunately, most of the pediatric studies have not described the specific CT patterns [12–15]. When describing the findings, a number of terms or descriptors have been mentioned, which are not standard for description of pulmonary lesions. As an example, in a large Chinese report, which was cited by Yang et al. [12], viral pneumonia-like changes were stated in 70.4% of 134 children undergoing chest imaging, with no specific characterization. Another study by Yu H. [59] with 82 pediatric COVID-19 patients reported unilateral pneumonia (46.34%), bilateral pneumonia (36.59%), multiple mottling (21.95%), partial pulmonary consolidation (3.61%), and lung texture enhancement (14.63%). However, no additional description was mentioned on these undefined terms. Hence, these values might underestimate the true characteristic radiologic patterns of pediatric COVID-19 infection. Chen J [14] preliminary report found GGOs and local patchy shadowing as the most common changes of chest CT scan. However, neither the detailed description nor the specific proportions were not fully explained again. Tang preliminary data on 26 children [13] demonstrated 7 (about 27%) cases with bilateral pulmonary infiltration, and 11 patients (about 42%) as unilateral pulmonary infiltration, but the detailed characterization was not described either (Figs. 2–4).

Generally speaking, GGOs, patchy consolidations and a combination of these (GGOs with superimposed consolidation) were the most common CT findings found in pediatric population with COVID-19 pneumonia. A large study by Lu X et al. [10] analyzed data from 171 children who had been confirmed to have COVID-19 infection. They reported bilateral GGO as the most common radiologic findings (37.3% of COVID-19 children), while 18.7% and 12.3% of infected children revealed local and bilateral patchy shadowing, respectively. Only in one study by Zhang [45] GGO was reported to be rare in pediatric patients (2.94%).

Halo sign was mentioned by some studies as a typical finding in children [15–18]. Xia [16] proposed consolidations with surrounding halo sign (as noted in 50% of cases) as the typical CT sign of the disease in pediatric COVID-19. Rahimzade et al [18] found diffuse air-space shadowing-patchy consolidation with halo-sign and ground-glass appearance in both lung fields, reflective of similar findings as to the adults.

Two cases with crazy paving pattern were also reported in one study [24]. Only 2 cases with pleural effusion and one white lung were reported, which were found among critically ill cases. Sun D [25] studied eight severe/critically ill patients with COVID-19 at the Intensive Care Unit (ICU), Wuhan. Chest imaging showed multiple patch-like shadows in seven patients and ground-glass opacity in six. All patients had abnormalities in chest CT or radiographs. Six cases had bilateral and two had unilateral pneumonias. Imaging changes included multiple patch-like shadows (7/8), GGO (6/8), pleural effusion (1/8) and white lung-like change (1/8). The other studies revealed no evidence of white lung, pleural effusion, and pneumothorax in children with COVID-19, probably due to milder inflammatory changes in this age group. Hence, the CT imaging manifestations correlate with

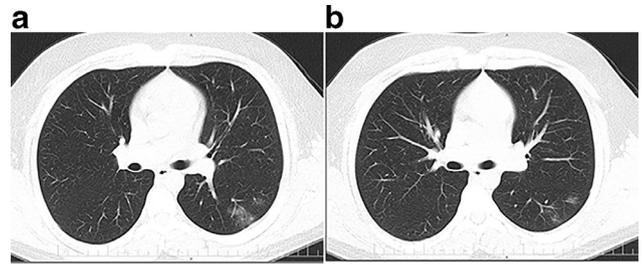


Fig. 2. A 14-year-old boy who presented with fever, malaise, and cough for a few days. CT images show small subpleural ground-glass opacifications (GGO) in the left lower lobe.

the disease activity and severity in the children with COVID-19 pneumonia.

In one study by Chen A [23] on 14 children, bronchial wall thickening was a common finding in children compared to adults. In this report, GGOs accounted for 42.9% (3/7), bronchial wall thickening occurred in 28.6% (2/7), and GGOs with superimposed consolidations and nodular opacities in 14.3% (1/7). These CT features did not differ in two groups, except for bronchial wall thickening, which was more commonly found in pediatric patients ($p = 0.048$).

Distribution

In terms of distribution patterns, most of the studies described peripheral distribution as the most prominent finding in children, though a certain proportion was not explained [17,20,21]. Only one retrospective analysis by Liu H et al. [22] reported the pulmonary involvement in four COVID-19 children to be of non-specific abnormalities (pure GGOs or consolidations) distributed without peripheral predominance, unlike the adults. This suggests that distribution pattern of COVID-19 in children might sometimes vary. Also, they reported more severe findings when COVID-19 is superimposed with other pathogen infections. A 2-month-

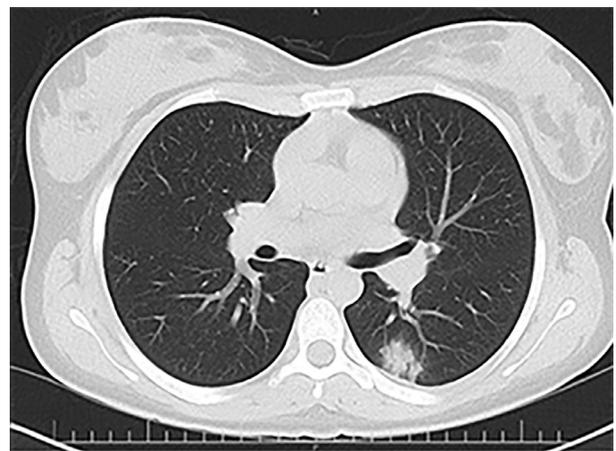


Fig. 3. A 14-year-old girl with COVID-19. CT image shows focal subpleural Ground-glass opacifications (GGO) with superimposed consolidation in the left lower lobe.

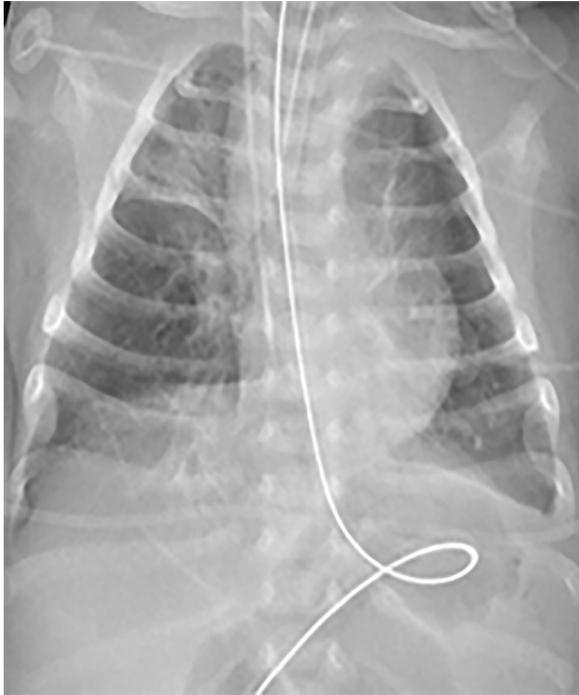


Fig. 4. A 3-week-old boy presented with a 2-day history of tachypnea, nasal congestion, and reduced feeding. Reverse-transcriptase-polymerase-chain-reacting testing of nasal swabs to detect SARS-CoV-2 were positive on day 7 after presentation. Chest radiograph demonstrates partial right upper lobe atelectasis and bilateral central streaky opacities.

old infant with simultaneous RSV and SARS-CoV-2 infections had multiple focal consolidations and pleural effusion.

Among the studies which had determined the detailed distribution characteristics (16 studies), 100 patients (55%) had unilateral, and 81 cases (45%) had bilateral pulmonary involvement, somehow consistent with the study of Tang et al. [13] who found 42% unilateral versus 27% bilateral pulmonary infiltrations in these patients. They proposed that the CT manifestations of children might be quite different from those of adults, in which bilateral manifestations are more common [29].

Clinical course and CT abnormalities

Some studies have described the correlation between clinical course and chest CT findings in COVID-19 in pediatrics. Normal CT scans were found in children with milder disease [26] in a study by Qiu H. They evaluated 36 COVID-19 children, 19 (53%) of which had pulmonary GGOs on CT scan, in favor of atypical pneumonia. None of the children with mild disease had CT changes. By contrast, 19/19 (100%) of patients with moderate disease had GGO. However, in most studies, children with COVID-19 infection were reported to have a mild clinical and radiological disease. Li W et al. [21] found very modest peripheral abnormalities on the CT scans of these patients, mainly in the form of patchy ground-glass opacification, all of which disappeared on follow-up exams.

The role of chest imaging

The significance of chest imaging for early detection and follow-up of COVID-19 infection in pediatrics was demonstrated by Wang [20]. In a retrospective study on 31 children, they found fourteen cases (47%) with abnormal chest CT (typical peripheral patchy GGOs and nodules), mostly located in the bilateral lower lobes with a subpleural predominance. Among 14 patients, two cases with typical chest CT changes had a negative nasopharyngeal swab test before the diagnosis had been made. This emphasizes the significance of combined epidemiological history and typical CT features to select patients who need repeated PCR-testing. Furthermore, in three cases who did not have clinical symptoms, typical chest imaging findings were present. Also, during the recovery period, with the improvement of the clinical symptoms, the imaging findings gradually decreased. In two children, the pulmonary lesions in chest CT were completely resolved. Overall, this study provides evidence for the importance of chest imaging in children with COVID-19 pneumonia for early detection of infection and follow-up.

Moreover, in the study of Wang et al. [20], two infants were reported who revealed atypical radiologic manifestations. Atypical lung manifestations in infants and neonates have also been reported in few other case reports [27,28,42]. It has been also suggested that bedside radiographs can be employed for follow-up evaluation of COVID-19 infection in very young children, in order to reduce the radiation burden of chest CT scan. However, in some other studies, the importance of dynamic combined re-examination with both PCR-testing and chest CT scan in pediatric COVID-19 patients has been emphasized [17]. Indeed, these studies believe PCR and CT scan hold complementary roles in the detection and follow-up evaluation of pediatric patients.

DISCUSSION

With COVID-19 disease spreading globally, the number of children diagnosed with COVID-19 infection has increased notably. While the vast majority of pediatric patients occur in familial clusters and have mild clinical symptoms, several cases have been reported with severe events or even death. Furthermore, children with COVID-19 are potential sources of community transmission. These issues highlight the importance of careful investigation of children with suspected infection for the early detection, not only to protect children with underlying diseases, but also to enhance the protection of their close contacts.

COVID-19 diagnosis is generally based on clinical symptoms and contact history combined with laboratory testing and radiological studies. In adults, PCR and chest CT can be applied interchangeably [50–53]. Chest imaging in adults offers valuable information not only in the initial diagnosis of COVID-19, but also in monitoring disease progression and efficacy of response to treatment. Peripherally located multifocal ground-glass opacities have been reported to be the earliest and typical CT manifestation in adults with COVID-19

[51–53]. With disease progression, superimposition of consolidation on ground-glass opacities is seen. However, in children, the CT findings are generally mild and due to its high radiation burden, the exact role of early chest CT imaging remains unknown. Some authors have proposed that chest imaging abnormalities in children may sometimes be evident even before than clinical manifestation of COVID-19, and thus early CT imaging may play an important role in the timely detection of these asymptomatic carriers. As a tangible example, Wang D. [20] reported three COVID-19 children with no clinical symptoms who had typical chest imaging findings. Albeit, due to modest CT findings in pediatric population, a balance should be struck between the risk of radiation and the necessity for CT scan. Moreover, it should be noted that in pediatric population, a low-dose chest CT appears more suitable in order to reduce radiation exposure [60]. Indeed, a combination of pathogen detection (using RT-PCR) and chest CT imaging should be considered when managing symptomatic pediatric patients. A positive contact history, fever, or respiratory symptoms should raise the possibility of SARS-CoV-2 infection. Then, careful dynamic monitoring with early and follow-up chest imaging, in conjunction with clinical assessment and laboratory tests, may be helpful for early detection of COVID-19, timely isolation, and early treatment. Especially those children who have infected family members should be monitored, and family clustering should be reported to ensure a timely diagnosis. Thus, regarding the value of chest CT in the management of COVID-19, being familiar with its early and typical diagnostic features of clinically suspicious children offers a valuable chance to fight against the disease spread.

In this systematic review, we found that most children with COVID-19 demonstrate similar radiological manifestations as to adults, except for a higher percentage of normal scans (26%). Ground-glass opacities and consolidations were found as the main characteristics of SARS-CoV-2 infection in pediatric patients. Other reported findings include halo sign, pulmonary nodules, bronchial wall thickening, and crazy-paving sign. Undetermined interstitial changes and bronchial pneumonia-like changes are also reported in literature, however, these terminologies are vague and not defined in detail for reproducibility. Pulmonary findings on pediatric imaging studies were often milder compared to adults, probably indicating a milder inflammatory response induced by COVID-19 in this population. In most children, the lung manifestations are mild and focal, unless a concomitant pathogen or an underlying disease existed, which would complicate the situation [61–63]. Most studies found peripheral distribution to be a prominent finding in children, although one small study found that ground-glass opacifications and consolidations in children may not have peripheral distribution [22]. Of pediatric patients with a described distribution pattern, 55% had unilateral pulmonary findings, as opposed to adults in which a bilateral distribution is more common. In most studies, chest imaging was utilized for the follow-up management of children with COVID-19, all of which were consistent with

clinical symptoms, and most of the abnormal CT findings eventually improved.

Moreover, it should be noted that higher incidence of normal CT or frequent asymptomatic/oligosymptomatic pediatric COVID-19 cases might also underline the importance of early detection of the disease in this specific population. These cases carry potentially infectious SARS-CoV-2 particles in their nasal secretions and stool for a long time, which likely contributes to early disease transmission to close contacts. Interestingly, it has been shown that asymptomatic patients might even have a significantly longer duration of viral shedding compared to symptomatic cases [34,39].

Our study suffers from few limitations. Firstly, there are only few published studies on radiologic manifestations of COVID-19 in pediatric population, and many of these are limited by small sample sizes. Secondly, the lack of consistency in the CT descriptors terms among the available articles might interfere with definite judgment and interpretation in some cases. Using common lexicon and descriptors would not improve the interdisciplinary communication of abnormal imaging findings and facilitating the diagnostic management of patients different diseases (including COVID-19), but also helps in conducting future research and systematic reviews more effectively [64–67]. Thirdly, the indications of CT imaging in many articles were not clearly described, which may describe the lower positive predictive value of chest CT in this population compare to adults. Finally, CT imaging is mostly performed in symptomatic patients, while many COVID-19 children manifest no significant clinical symptoms. Thus, the results of the reported studies might have been potentially affected by this bias. Therefore, due to the limited number of pediatric patients with COVID-19, the specific definitions and management strategies for this group have not yet been fully explored, which highly warrant further long-term investigations in this field.

CONCLUSION

This review of available studies of COVID-19 pneumonia in pediatric patients provides insight into the initial and follow-up CT imaging findings of the disease in this specific population. The most common CT findings were ground-glass opacities, consolidation, or a combination of these, typically with lower-lobe predominance. According to our review, along with epidemiological suspicion and contact tracing, (preferably low-dose) chest CT can be employed in the early diagnosis and management of selected symptomatic pediatric patients, if clinically warranted.

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